**Remarks**

The April 26, 2005 Official Action has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set in the April 26, 2005 Official Action. Therefore, the initial due date for response was July 26, 2005. A petition for a one month extension of the response period is presented with this response, which is being filed within the one month extension period.

At pages 4 and 5 of the instant Official Action, the Examiner has objected to the specification on three grounds. First, the Examiner has objected to Table I for lacking a clear description of the sequence portions in Table I. In response, Applicants have amended Table I to clearly describe that SEQ ID NO: 1 is nucleotides 1-30,000, SEQ ID NO: 2 is nucleotides 30,001-60,000, SEQ ID NO: 3 is nucleotides 60,001-90,000, and SEQ ID NO: 4 is nucleotides 90,001-103,600 of the monensin biosynthetic gene cluster.

Second, the Examiner has objected to the amendment submitted January 25, 2005 under 35 U.S.C. §132(a) for allegedly introducing new matter. Specifically, the Examiner contends that PCT/GB/02072 was not incorporated in the specification as originally filed. Applicants note that the instant application is a §371 application of PCT/GB00/02072. However, in the interest of expediting prosecution, Applicants have deleted the reference to incorporating the PCT application from the instant specification.

Third, the Examiner contends that there are some inconsistencies within Table I. Applicants have amended to Table I to address inconsistencies a) through o) identified by the Examiner. Support for the amendments can be found, for example, at Table II.

In light of all of the foregoing, Applicants respectfully submit that the Examiner's objections to the specification have been overcome and respectfully request that the objections be withdrawn.

At pages 5-7 of the instant Official Action, the Examiner has objected to certain claims on the following two grounds. First, the Examiner has objected to claims 9, 31, 32, and 47 under 35 C.F.R. §1.75(c) for allegedly failing to further limit the subject matter of a previous claim. Applicants have cancelled claims 9 and 47 for the reasons set forth below, thereby rendering the instant objection moot. With regard to claims 31 and 32, Applicants submit that the loading module, extension modules, or domains recited in claim 30, from which claims 31 and 32 depend, can be a module or domain from a monensin polyketide synthase (as recited in claim 31) or a module or domain from a polyketide synthase of a polyketide other than monensin (as recited in claim 32). Inasmuch as the features recited in claims 31 and 32 are distinct, Applicants submit that the instant objections under 35 C.F.R. §1.75(c) are untenable and respectfully request their withdrawal.

Second, the Examiner has objected to claims 1, 3, 11, and 46 on formal grounds. Applicants have cancelled claim 46 for the reasons set forth below and have amended claims 1, 3, and 11 to incorporate the Examiner's suggestion with regard to the use of "encodes" instead of "encodes for." Accordingly, Applicants respectfully submit that the Examiner's objections to claims 1, 3, 11, and 46 are untenable and respectfully request that the objections be withdrawn.

At pages 9-13 of the instant Official Action, the Examiner has rejected claims 1, 2, 4, 5, 7-12, 30-34, 37, 38, and 46-49 under 35 U.S.C. §112, second paragraph for alleged indefiniteness.

Claims 5, 31, and 46 have been rejected for allegedly failing to satisfy the written description

requirement of 35 U.S.C. §112, first paragraph.

Claims 1, 7, 9-11, 30-33, 35, 37, 38, and 47-49 have been rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative under 35 U.S.C. §103(a) as unpatentable over WO 98/01546.

Lastly, the Examiner has rejected claim 12 under 35 U.S.C. §103(a) as unpatentable over WO 98/01546.

The foregoing objections and rejections constitute all of the grounds set forth in the April 26, 2005 Official Action for refusing the present application.

In accordance with the present amendment, claims 9, 46, and 47 have been cancelled. Applicants have also amended claims 1-5, 8, 11, and 30-34. Applicants submit that support for the amendments to claims 3-5, 8, 11, and 31-33 is inherent in the claims as previously presented. Support for the amendment to claim 34 can be found, for example, at page 30, lines 5-9. Support for the amendment to claim 2 can be found, for example, at page 40, lines 16-17. Support for the amendment to claims 1 and 30 can be found, for example, in original claim 8 and Tables I and II.

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

For the reasons set forth below, Applicants respectfully submit that the various objections to the specification and claims, the 35 U.S.C. §112, second paragraph rejections of claims 1, 2, 4, 5, 7-12, 30-34, 37, 38, and 46-49, the 35 U.S.C. §112, first paragraph rejections of claims 5, 31, and 46, the 35 U.S.C. §102(b)/§103(a) rejection of claims 1, 7, 9-11, 30-33, 35, 37, 38, and 47-49, and the 35 U.S.C. §103(a) rejection of claim 12, as set forth in the April 26, 2005 Official Action, either lack merit or cannot be maintained in view of the present amendment. These grounds of objection and rejection are, therefore respectfully traversed.

**CLAIMS 1, 2, 4, 5, 7-12, 30-34, 37, 38, AND 46-49, AS AMENDED, SATISFY THE REQUIREMENTS OF 35 U.S.C. §112, SECOND PARAGRAPH**

The Examiner has rejected claims 1, 2, 4, 5, 7-12, 30-34, 37, 38, and 46-49 under 35 U.S.C. §112, second paragraph for alleged indefiniteness on the following ten grounds.

First, the Examiner contends that claims 30-34, 37, and 38 are indefinite for reciting "**an** erythromycin loading module." Applicants have amended claim 30, from which claims 31-34, 37, and 38 depend, to recite "**the** erythromycin loading module," thereby obviating the instant rejection.

Second, claim 34 has been rejected for alleged indefiniteness for recitation of the phrase "derived from." Specifically, the Examiner contends that it is unclear in which ways the KSq domain can be "derived." In the interest of expediting prosecution, Applicants have amended claim 34 to recite that the KSq domain is derived by mutating the active site cysteine residue to a glutamine. Support for this amendment can be found throughout the specification including, for example, page 30, lines 5-9.

Third, the Examiner has rejected claims 1, 7-12, and 46-48 for being generally unclear. Applicants have adopted the Examiner's suggested claim language for claim 1, from which claims 7-12 and 46-48 depend, to eliminate any ambiguity perceived by the Examiner.

Fourth, the Examiner contends that the phrase "the complete monensin gene cluster," recited in claim 2, is indefinite. Applicants have amended claim 2 to recite that the monensin gene cluster encodes for all of the gene products set forth in Table II. Support for this amendment can be found at, for example, page 40, lines 16-17.

Fifth, it is the Examiner's position that the metes and bounds of the phrase "at least a part of one or more of the following genes" in claim 4 are unclear. Applicants have

amended claim 4, from which claim 5 depends, to recite "at least one of the following genes," thereby eliminating any perceived ambiguity in the claim.

Sixth, the Examiner contends that the nature of a "DNA sequence encoding any one or more of the domains as set out in Table 1" in claim 8 is confusing. Applicants have amended claim 8 to recite a "DNA sequence encoding any one or more of the domains and gene products as set out in Table I." Applicants respectfully submit that claim 8, as amended, is clearly drawn to DNA sequences encoding the domains of the polyketide synthases listed in Table I as well as the polypeptide encoded by the genes set forth in Table I. The claimed DNA sequences need not be the exact portion of SEQ ID NOs: 1-4 as set out in Table I, but rather the claimed DNA sequences encode the polypeptide encoded by the gene sequence provided in Table I. Accordingly, Applicants submit that amended claim 8 satisfies the requirements of 35 U.S.C. §112, second paragraph.

Seventh, with regard to claims 9 and 47, it is the Examiner's position that it is "confusing on how such short sequences can retain the activities as required in claim 1." Without agreeing with the Examiner's position and in the sole interest of expediting prosecution of the instant application, Applicants have cancelled claims 9 and 47, thereby rendering the instant moot.

Eighth, the Examiner has rejected claim 30 and dependent claims 31-34, 37, 38, and 49 because the overall claim structure of claim 30 is allegedly very confusing. Applicants have employed the Examiner's suggested claim language as a guide for claim 30, thereby overcoming the instant rejection. Support for reciting the ethylmalonate specific and malonate specific acyl transferase domains can be found, for example, at Table I.

Ninth, claim 33 and dependent claim 34 have been rejected because it is the Examiner's position that the phrase

"adapted to load" is confusing. Applicants have eliminated this phrase from claim 33, thereby rendering the instant rejection moot.

Lastly, the phrase "said monensin extension module" in claim 49 allegedly lacks antecedent basis. Applicants respectfully disagree with the Examiner. Claim 49 depends directly from claim 34 which recites a "KSq domain derived from a ketosynthase (KS) domain of a **monensin extension module**." Accordingly, Applicants submit that there is literal antecedent basis for the phrase "said monensin extension module" in claim 49.

In light of all the foregoing, Applicants submit that each of the rejections of claims 1, 2, 4, 5, 7-12, 30-34, 37, 38, and 46-49 under 35 U.S.C. §112, second paragraph for alleged indefiniteness has been overcome. Accordingly, Applicants respectfully request that the rejections be withdrawn.

**CLAIMS 5, 31, AND 46, AS AMENDED, SATISFY THE WRITTEN DESCRIPTION REQUIREMENT OF 35 U.S.C. §112, FIRST PARAGRAPH**

The Examiner has rejected claims 5, 31, and 46 for allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph.

With regard to claims 5 and 31, it is the Examiner's position that the specification fails to adequately describe an "allele, mutation, or other variant" of the instantly claimed domains and modules. Applicants respectfully disagree with the Examiner. However, in the interest of expediting prosecution, Applicants have amended claims 5 and 31 to eliminate reference to alleles, mutations, and variants thereof, thereby rendering the instant rejection of claims 5 and 31 moot.

With regard to claim 46, it is the Examiner's position that claim 46 is drawn to a "DNA product encoding a

variant having a 90% sequence identity to MonAIV (also having exactly one domain - or active fragment thereof - of SEQ ID NO: 22)." The Examiner contends that the instant specification fails to fully describe a genus that has sequence identity limitations in the absence of functional limitations. Applicants respectfully disagree with the Examiner, but have cancelled claim 46 in the interest of expediting prosecution of the instant application.

In light of the foregoing, Applicants submit that each of the rejections of claims 5, 31, and 46 for allegedly failing the written description of 35 U.S.C. §112, first paragraph for alleged indefiniteness have been rendered moot. Accordingly, Applicants respectfully request that the rejections be withdrawn.

**CLAIMS 1, 7, 9-11, 30-33, 35, 37, 38, AND 47-49 ARE NOT ANTICIPATED OR RENDERED OBVIOUS BY WO 98/01546**

Claims 1, 7, 9-11, 30-33, 35, 37, 38, and 47-49 have been rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as unpatentable over WO 98/01546 (hereinafter Leadlay et al.). It is the Examiner's position that Leadlay et al. teach the use of AT5 of MonAIV in place of the AT domain of the first extension module of the erythromycin (ery) polyketide synthase (PKS) comprising the ery loading module, the first and second extension modules of the ery PKS, and the ery thioesterase. The Examiner acknowledges that Leadlay et al. does not explicitly recite that the AT domain is AT5 of MonAIV. Indeed, Leadlay et al. refer to the AT domain obtained from the monensin PKS as ATX. However, the Examiner contends that the disclosure within Leadlay et al. requires that the AT domain be the ethylmalonyl-specific AT5 domain of the monensin PKS from *S. cinnamonesis*.

Applicants respectfully disagree with the Examiner's

position in this regard. In any event, independent claims 1 and 30 are patentably distinguishable from Leadlay et al. in view of the present amendment which requires that when the recited fragment or domain of MonAIV is the ethylmalonate specific acyl transferase, the domain or fragment has the sequence of amino acids 592 to 932 of SEQ ID NO: 22. Support for this amendment can be found throughout the specification including, for example, original claim 8 and Tables I and II. Original claim 8 is drawn to a DNA sequence encoding any of the domains set out in Table I. Table I, at line 49 indicates the AT5 domain, which is ethylmalonate specific, starts at nucleotide 44221 and ends at nucleotide 45243. A review of the nucleotide sequence of MonAIV and the amino acid sequence of MonAIV provided in Table II (specifically SEQ ID NO: 22) reveals that the AT5 domain is amino acids 592 to 932 of SEQ ID NO: 22.

Applicants respectfully submit that Leadlay et al. fail to disclose a nucleic acid molecule which encodes amino acids 592 to 932 of SEQ ID NO: 22. Even if it is assumed that the Examiner is correct in her assertion that the monensin nucleotide sequence inserted into the ery PKS in Leadlay et al. has AT5 activity, it is clear that the nucleotide sequence employed does not encode amino acids 592 to 932 of SEQ ID NO: 22. Indeed, Leadlay et al. state at page 100, line 16 that the monensin nucleotide sequence amplified was approximately 900 basepairs. Significantly, the nucleotide sequence encoding amino acids 592 to 932 of SEQ ID NO: 22 is over 1000 basepairs in length (see Table I). Additionally, a review of the primers utilized by Leadlay et al. to amplify the ATX segment of monensin do not hybridize around the start and end nucleotide sites of AT5 as set forth in Table I. Accordingly, a thorough review of Leadlay et al. makes clear that it fails to teach the instantly claimed nucleotide sequences.

In addition to the passages cited for support hereinabove, Applicants also submit that the present

amendments to claims 1 and 30 cannot be regarded as introducing new matter when considered in light of In re Johnson, 194 U.S.P.Q. 187 (CCPA 1977), which stands for the proposition that an applicant for patent may narrow the claims to avoid having them read on subject matter which applicant may not be entitled to claim.

In light of all the foregoing, Applicants respectfully request the withdrawal of the rejection of independent claims 1 and 30 and dependent claims 7, 9-11, 31-33, 35, 37, 38, and 47-49 under 35 U.S.C. §102(b) as anticipated by or, in the alternative under 35 U.S.C. §103(a) as unpatentable over WO 98/01546.

**CLAIM 12 IS NOT RENDERED OBVIOUS BY WO 98/01546**

Claim 12 has been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over WO 98/01546 (hereinafter Leadlay et al.). For the reasons set forth above, Applicants submit that Leadlay et al. fails to teach or suggest each and every limitation of claim 1, from which claim 12 depends. Accordingly, Applicants respectfully submit that the rejection of claim 12 under 35 U.S.C. §103(a) is untenable and respectfully request the rejection be withdrawn.

**CONCLUSION**

In view of the amendments presented herewith, and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the April 26, 2005 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,
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